LSAH

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Association between age and PSA values

Male participants in the LSAH have been offered prostate-specific antigen (PSA) screening since 1993. The results of these tests are used, on an individual basis, to assess the need for more extensive screening for prostate cancer. The LSAH now has enough group data to provide population information about the normal ranges of the test values and the variation in values associated with age.

The normal range of values is generally considered to be 0 to 4 ng/mL (nanograms per milliliter of serum), with higher values prompting further investigation and testing. However, questions have been raised about the upper level of this standard because a significant number of older men in the general population, whose values exceed the range, may have received more extensive testing than necessary.

Age-specific ranges have been suggested for improved sensitivity and specificity. The sensitivity of a screening test is the probability of a case being identified by the test. The specificity of a screening test is the probability of correctly identifying a person as disease free. Prostate cancer generally progresses slowly and is more likely to make a major health impact when it occurs at a young age than when it occurs in old age. The sensitivity of the screening test is, therefore, more important among younger men and the specificity is more important among older men.

To determine the association between age and PSA values, a study was conducted among 422 healthy men age 40 to 79 years in Olmsted County, Minnesota [1]. These men were determined to be free of prostate cancer, based on detailed clinical examinations that included a digital rectal examination, PSA testing, and a transrectal ultrasound.

The values of the PSA testing correlated directly with age. The distribution of the values was examined and the 95th percentile was identified for each age decade. The use of the 95th percentile value in the disease-free portion of a population would, conceptually, result in 95 percent of disease free men being correctly identified as disease free and 5 percent of disease free men at all ages would be subject to further testing. This study did not address the converse; that is, they did not examine diseased men to determine what percent of that population would have PSA values within the normal range and, therefore, might not be referred for further testing.

We identified the age-specific distribution of PSA values among the LSAH participants, both astronaut and comparison, and identified what percent of this population would not be routinely referred for further testing using the age-specific-range of values recommended by the Olmsted County study. For the purposes of this report, we used PSA values only. Therefore, the comparison is between a disease-free (Olmsted County study) population and the LSAH population without any prior assumption being made about the disease status of the LSAH population. The most recent test for each individual was included in these analyses. A total of 428 men (295 comparisons and 133 astronauts) have PSA results from their most recent physical examination. The table above shows the percent of the LSAH population who had values within the age-specific range recommended by the Olmsted County Study. As you can see, the LSAH results are very similar to those of the Olmsted County study.

Percent of LSAH Participants with PSA values within the age-specific ranges recommended by the Olmsted County study based on 95th percentile values

	Olmsted County	Astronauts		Comparisons		Total	
Age (years)	Age-specific Range	n	%	n	%	n	%
40-49	0 – 2.0	65	100.0	45	88.9	110	95.5
50-59	0 – 3.0	39	97.4	190	93.2	229	93.9
60-69	0 – 4.0	27	96.3	60	91.7	87	93.11
70-79	0 – 5.5	*		*		2	

**Data for two participants in the 70-79 age range were excluded because of the small number of cases*

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[1] Oesterling, et al. Free, complexed and total serum prostate specific antigen: the establishment of appropriate reference ranges for their concentrations and ratios. Journal of Urology. 154(3):1090-5,1995

Melatonin: A Snapshot

Melatonin, an ancient chemical produced by animals and plants, recently has been hailed in the lay press as a "natural wonder drug." Claims for its "miraculous" properties have ranged from curing jet lag to fighting disease. What is melatonin? Is there any basis for these and other still more eye-catching claims?

Melatonin is a chemical that is produced internally by life forms, from humans to one-celled algae. All living creatures seem to generate this powerful substance in rhythmic patterns, with more melatonin being produced at night than during the day. In humans and animals, even very small amounts of melatonin tend to have tranquilizing, sleep-inducing effects. Melatonin seems to have an effect opposite to adrenalin, another well-known hormone. Thus, adrenalin's message to the body is "fight or flee;" melatonin's message is "rest and recover."

Dynamics of melatonin in the body: In humans, melatonin is made from the essential amino acid tryptophan, which is present in many foods and food supplements. Our bodies convert tryptophan to serotonin, a so-called "mood chemical," which in turn is converted into melatonin. Humans produce 5 to 10 times more melatonin at night than during the day, which has led some to call it the "chemical expression of darkness." Melatonin levels tend to peak early in the morning, usually between 2:00 and 4:00 a.m. (Figure 1). Even though all healthy humans produce melatonin, the amounts they produce over the course of a day vary greatly depending on how old they are. Babies begin producing increasing amounts of melatonin starting from three months or so, when their sleep patterns begin to synchronize with day-night cycles. Young children produce the most nighttime melatonin, with the greatest amounts produced before puberty, at which time the nighttime peaks begin to fall, and continue to decline throughout adulthood. Although older people still have day-night melatonin cycles, the amounts of melatonin they produce at night become quite small after age 60 (Figure 2).

Figure 1. *The 24-hour Cycle of Melatonin Production*

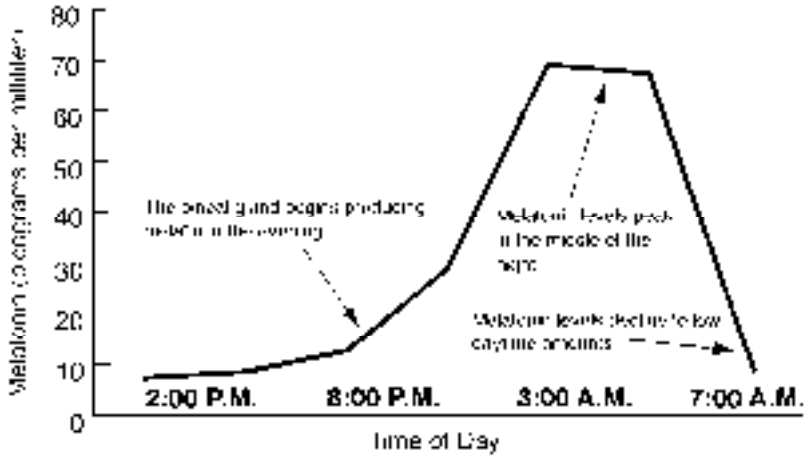
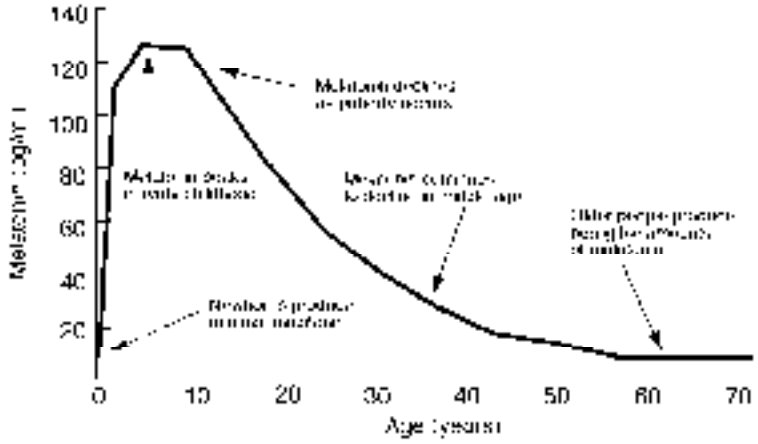


Figure 2. *Nocturnal Melatonin Levels Throughout the Life Span*



Taken by mouth as a tablet, capsule, or liquid, melatonin is broken down quickly by the liver before much of it can reach the bloodstream. The kidneys, too, remove melatonin and its breakdown products quickly, so that half of the dose taken disappears from the body in less than an hour.

Proposed uses for melatonin: Although advocates have proposed many uses for melatonin, very little clinical evidence has been found to substantiate these claims. The most frequently suggested use of melatonin so far has been in treating jet lag, insomnia, or other sleep disorders. Accordingly, the most common (and best accepted) use of melatonin is to "reset" the sleep-wake cycle after

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disruptions such as jet lag or shift-work. Such treatments should last no longer than a week or two.
Some recent research suggests that melatonin may act as an antioxidant, and may enhance the functioning of the immune system. Some researchers recommend melatonin supplements to reverse aging, fight disease, and relieve stress in people older than about 45 years. Others suggest that people at high risk for heart disease or cancer begin taking melatonin supplements in their mid-30s. Melatonin supplements also are thought by some to improve the health and energy of geriatric patients. These claims have yet to be proven, or disproven, with well-controlled clinical trials.

Children and young adults in particular should avoid chronic (long-lasting) use of melatonin, since their bodies produce sufficently high amounts of this substance naturally.

Melatonin in the marketplace: The FDA does not classify melatonin as a pharmacological agent, i.e., it is not regulated by any federal agency, nor is it considered an accepted treatment for any specific disease. Thus, melatonin of varying strength and impurity is sold freely in health-food stores and pharmacies. Several companies produce melatonin for human consumption; different brands offer different doses and dosage forms (tablets, capsules, or sublingual disks). Tablets, the most common form, come in 1, 2, 3, or 5 mg doses.

Dosage and regimen: The general philosophy behind choosing a melatonin dose is to boost the individual's circulating nighttime melatonin levels to a level that came naturally when that person was younger or was sleeping normally. Thus, the melatonin dose and regimen for taking it depends on the subject's age and the intended use of the chemical. In general, to promote sleep or to "reset" circadian rhythms (especially for going to sleep earlier and waking up earlier), 1 mg to 5 mg doses by mouth are given before bedtime as tablets or capsules. Before-bedtime doses are always preferable to avoid drowsiness while the person is awake. The dose can be discontinued without any problems when the sleep and rhythm disturbances resolve.

These are exciting times for melatonin researchers around the world. If these "miraculous" claims ascribed to melatonin supplements are verified, then melatonin may indeed turn out to be a "natural wonder drug." The mad rush to health-food stores, pharmacies, and book stores attests to the excitement of possibly capturing some of the vigor of the "wonder years." As always, the most conservative course is caution during the wait for sound, well-verified clinical proof of melatonin's effectiveness in these applications.

Nail disease

Onychomycoses represent the most frequently seen nail diseases and are among the most difficult to treat. Onychomycoses of the nails include fungal infections caused by pathogens that invade the nail plate and may be primary infections, or may be secondary to infections in other areas around the nails. These infections are rare in children and increase in incidence with age.

The prevalence (number of cases at a point in time) has been estimated to be approximately 4.7 percent in adults in the United States older than age 55 . The incidence (number of cases identified over a period of time) among the elderly has been estimated to be 35 percent. These estimates in the general population are consistent with estimates for the LSAH population.

Most fungi cannot infect a healthy nail. Nails become susceptible to fungal infection when predisposing factors such as impaired blood circulation, peripheral neuropathy, diabetes, immune defects, and damage from repeated minor trauma are present. Minor trauma may be caused by an ill-fitting shoe, boot, or glove.

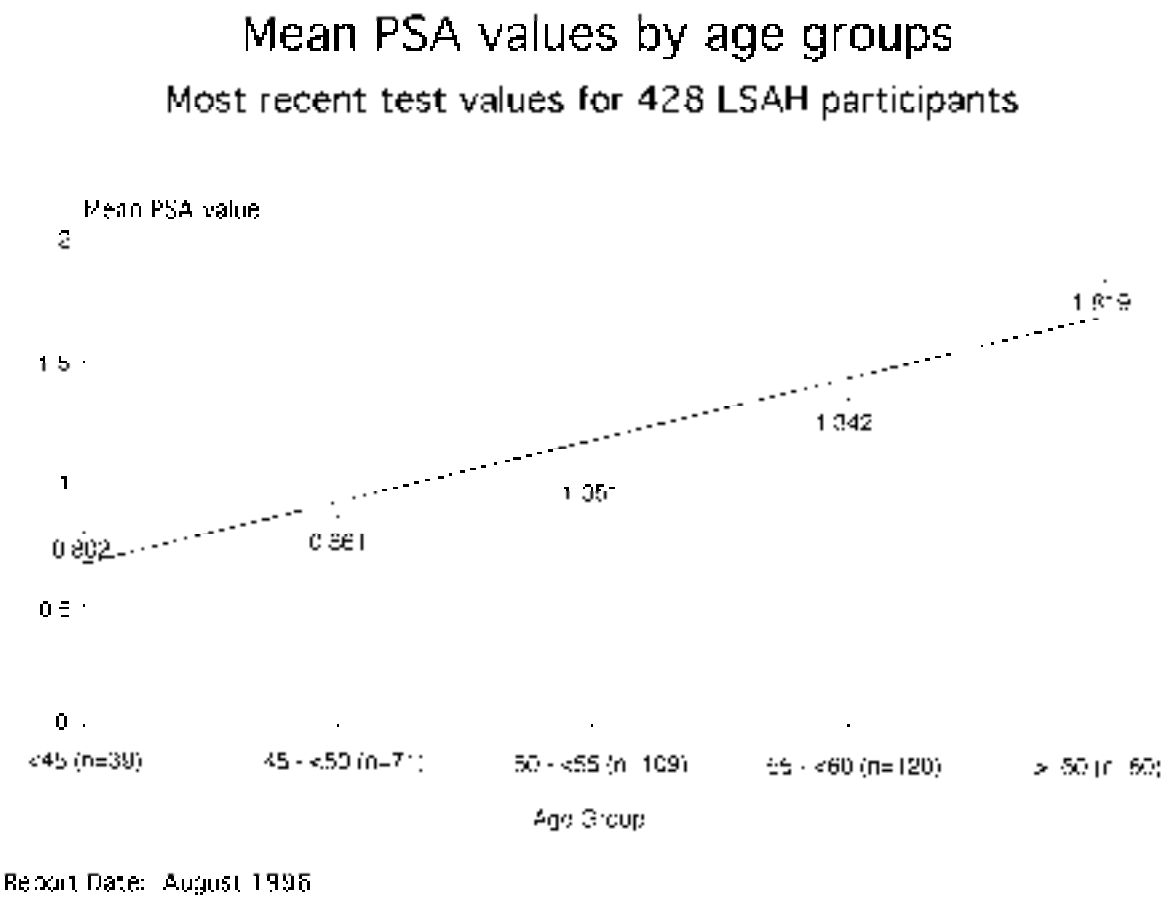
There are many patterns of infection, each pattern depending on the specific infecting agent. The nail plate may discolor and separate from the underlying bed as debris accumulates under the nail. It may thicken or become soft, dry, and powdery. One or more nails may be infected and toenails are more likely than fingernails to become infected.

There are several antifungal oral agents, none without some side effects, that have varying effectiveness in treating onychomycoses. These agents have been reported as being less than 40 percent effective in curing toenail infections. However, newer drugs that penetrate into the nail bed have tentatively reported cure rates as high as 80 percent. These newer drugs hold promise but are not fully investigated as yet.

Prevention remains the best option for control of onychomycoses. Preventive measures include good hygiene of the nails and surrounding areas and careful fitting of shoes and heavy work gloves.

PSA values – continued from page 1

PSA values for the LSAH participants are shown in the following graph. PSA testing is one tool, which is used with digital rectal examination, to screen men for prostate cancer. Based on the results of these tests, further testing may be recommended by the physician as appropriate.



For your information

If you want a copy of your exam results, please complete and sign a release form while you are visiting the Clinic for your examination.

The form is called Privacy Act Disclosure Authorization and Accounting Record (DAAR), or NASA Form 1536.

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